

REMARKS/ARGUMENTS

Claim 38 has been canceled. Claims 5-29, 31, 35, 37, 39-41 and 45-53 are active in the case. Claims 5-8, 11-15, 22-27, 31 and 47-49 stand withdrawn from consideration. Reconsideration is respectfully requested

The present invention relates to compounds that inhibit the activity of transcription factor AP-1.

Claim Rejection, 35 USC 112, First Paragraph

The Examiner rejects Claim 37, which is directed to a method of inhibiting AP-1, on the basis that the specification does not enable the method as claimed. However, applicants point out that Test Example 1 on pages 225 to 230 of the text gives a comprehensive description which shows examples of compounds within the scope of Claim 9 being effective for inhibiting AP-1. Moreover, the specification discloses a method of administering embodiments of the presently claimed compound on page 189, lines 11-27. Thus, the text of the present application provides ample enablement of compounds that inhibit the activity of AP-1. Accordingly, withdrawal of this aspect of the non-reference ground of rejection is respectfully requested.

The rejection of Claim 38 is overcome by the cancellation of the claim.

With respect to the rejection of Claim 39, applicants have now amended the claim by deleting reference to the prevention of an autoimmune disease. The claims is now directed to a method of treating an autoimmune disease, ample support for which can be found in Test Example 2 of the specification as set forth on pages 230 to 231 of the text. Test Example 2 demonstrates that the compound of Example 12, that is within the scope of Claim 9, is effective against Type II collagen-induced arthritis in mice. Type II collagen-induced arthritis is representative of autoimmune diseases. Therefore, it can be reasonably expected based on

Application No. 09/830,559  
Reply to the Office Action dated July 1, 2005

the results of Test Example 2 that the compounds that are within the scope of Claim 9 are effective for treating autoimmune diseases. Thus, the invention of Claim 39 is fully supported by the specification.

### Claim Amendments

Claim 16 has been amended in lines 8 and 9 in order to improve upon the syntax of the claim. The amendment does not introduce new matter into the case.

Claim 39 has been amended by deleting the aspect of the claim of an agent that prevents an autoimmune disease upon the administration of a compound or a salt thereof of Claim 9. Claim 39 is therefore limited to an agent for treating a subject suffering from an autoimmune disease by administration of a compound or a salt thereof of Claim 9.

### Prior Art Rejection

Claims 9, 10, 16-21, 28, 29, 35, 38-40 and 51-53 stand rejected based on 35 USC 102 as anticipated by Gapinski, U. S. Patent 5,235,064 and Cohen et al, U. S. Patent 5,434,186. This ground of rejection is respectfully traversed.

As to the matter of the rejection of Claims 9 and 10 over the indicated prior art, applicants have amended independent Claim 9 by deleting the hydrogen atom component of the definition of group of  $R^4$ . By this amendment the compounds of Claims 9 and 10 are believed distinguished over the cited prior art.

As to the rejection of Claims 16-21, the compounds of these claims are not anticipated by the cited prior art, because of the different positioning of substituent groups in the compounds and by the quantities of substituent groups within the molecules.

Application No. 09/830,559  
Reply to the Office Action dated July 1, 2005

As to Claims 16 and 17 specifically, it should be noted that substituents  $R^{3a}$  and  $R^{4a}$  of the compounds of Claims 16 and 17 are located in the meta- and para-positions of the molecule relative to substituent  $X^{1a}$ . By contrast, in the compounds identified by the Examiner in his rejection, the substituent on the phenyl ring of the benzoyl group is positioned ortho to the carbonyl group and not in the meta and para positions.

As to Claims 18 and 19 specifically, it should be noted that substituents  $R^{3b}$  and  $R^{4b}$  of the compounds of Claims 18 and 19 are located in the ortho- and meta-positions of the molecule relative to substituent  $X^{1b}$ . By contrast, in the compounds identified by the Examiner in his rejection, the single substituent on the phenyl ring of the benzoyl group is positioned ortho to the carbonyl group.

As to Claims 20 and 21 specifically, it should be noted that substituents  $R^{3c}$  and  $R^{4c}$  of the compounds of Claims 20 and 21 are each located in a meta-position of the molecule relative to substituent  $X^{1c}$ . By contrast, in the compounds identified by the Examiner in his rejection, the single substituent on the phenyl ring of the benzoyl group is positioned ortho to the carbonyl group.

Additionally, it should be noted that groups  $R^{3a}$  and  $R^{4a}$  of the compounds of Claims 16 and 17, groups  $R^{3b}$  and  $R^{4b}$  of the compounds of Claims 18 and 19 and groups  $R^{3c}$  and  $R^{4c}$  of the compounds of Claims 20 and 21 are not hydrogen. That is, the phenyl group always has two substituents. By contrast, in the compounds identified by the Examiner in his rejection, the benzoyl group has only a single substituent on the phenyl ring. Clearly, the subject matter of Claims 16-21 is not anticipated by the cited references.

As to the matter of the rejection of Claim 28, the compound thereof is novel over the cited art, because it differs from the compounds of the prior art with respect to type and position of the substituents as follows:

(i) Group  $R^{4g}$  of the compound of Claim 28 is located in the para-position relative to the linking group  $X^{1g}$ . By contrast, in the compounds identified by the Examiner in his rejection, the benzoyl group has only a single substituent on the phenyl ring which is located ortho to the carbonyl, i.e.  $X^{1g}$  group.

(ii) Furthermore, substituent  $R^{4g}$  is an unprotected or protected hydroxyl group, or it is an unsubstituted or substituted alkoxy group. By contrast, in the compounds identified by the Examiner in his rejection, the corresponding substituent is ethoxycarbonylmethyl or carboxymethyl. Therefore, from the viewpoint of substituents, the substituent groups of the compounds referred to by the Examiner are different from those which qualify as being within the scope of group  $R^{4g}$ . Clearly, Claim 28 is not anticipated by the cited prior art.

As to the rejection of Claims 29, 35, 39 and 40, each one of these claims is dependent upon the scope of the benzene derivative of Claim 9. Accordingly, because Claim 9 has been amended so as to eliminate inclusion of the specific compounds mentioned by the Examiner in his rejection of Claim 9, Claims 29, 35, 39 and 40 also do not include within their scope any of the compounds mentioned by the Examiner. Claims 29, 35, 39 and 40 are therefore not anticipated by the cited prior art.

As to the matter of the rejection of Claims 51 and 52, the compounds thereof are novel over the cited art, because they differ from the compounds of the prior art with respect the number of substituents and the positions of the substituents in the molecules as follows:

(i) As to Claim 51, it should be noted the groups  $R^{3b}$  and  $R^{4b}$  are located in an ortho-position and a meta-position, respectively, relative to linking group  $X^{1b}$ . By contrast, in the compounds identified by the Examiner in his rejection, the single substituent on the phenyl ring of the benzoyl group is positioned ortho relative to the carbonyl group.

(ii) As to Claim 52, it should be noted the groups  $R^{3c}$  and  $R^{4c}$  are both located in a meta-position relative to linking group  $X^{1c}$ . By contrast, in the compounds identified by the

Application No. 09/830,559  
Reply to the Office Action dated July 1, 2005

Examiner in his rejection, the single substituent on the phenyl ring of the benzoyl group is positioned ortho relative to the carbonyl group.

(iii) It also must be observed with respect to the  $R^{3b}$  and  $R^{4b}$  groups of Claim 51 and the  $R^{3c}$  and  $R^{4c}$  groups of Claim 52, that these groups are not hydrogen in any instance. By contrast, in the compounds identified by the Examiner in his rejection, the phenyl ring of the benzoyl group has only a single substituent. Clearly, the subject matter of Claims 51 and 52 is not anticipated by the cited references.

Finally, as to Claim 53, the compound thereof is novel over the cited art, because it differs from the compounds of the prior art with respect to type and position of substituents as follows:

(i) It should be noted the group  $R^{4g}$  is located in the para-position relative to linking group  $X^{1g}$ . By contrast, in the compounds identified by the Examiner in his rejection, the single substituent on the phenyl ring of the benzoyl group is positioned ortho relative to the carbonyl group.

(ii) Note also that substituent  $R^{4g}$  is an unprotected or protected hydroxyl group, or it is an unsubstituted or substituted alkoxy group. By contrast, in the compounds identified by the Examiner in his rejection, the corresponding substituent is ethoxycarbonylmethyl or carboxymethyl. Therefore, from the viewpoint of substituents, the substituent groups of the compounds referred to by the Examiner are different from those which qualify as being within the scope of group  $R^{4g}$ . Clearly, Claim 53 is not anticipated by the cited prior art.

Withdrawal of the anticipatory ground of rejection of the claims is respectfully requested.

Since Claims 9, 18, 20 and 28 are distinguished over the prior art that has been cited as noted in the discussions above, the objection to Claims 41, 45, 46 and 50 is overcome.

Application No. 09/830,559  
Reply to the Office Action dated July 1, 2005

It is believed that the application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

Customer Number  
**22850**

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.  
Norman F. Oblon

Tel: (703) 413-3000  
Fax: (703) 413 -2220  
(OSMMN 08/03)

NFO/FDV

  
\_\_\_\_\_  
Frederick D. Vastine, Ph.D.

Registration No. 27,013